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# Critical limits of laboratory results for urgent clinician notification

**Professor Dr Lothar Thomas**

*Kirschbaumweg 8, 60489 Frankfurt*
*E-mail: th-books@t-online.de*

Critical limits of laboratory results need urgent notification to the clinician because they are an indicator of a critical or even life-threatening condition of the patient.

The publications about this topic are mainly from the 1970s. Since then, many laboratory methods have been improved, new parameters have been added, and there have also been changes in the evaluation and treatment of diseases.

Against this background and at the request of the Ameri-can Medical Association, J.G. Kost [1] conducted a survey on critical pa-rameters in the USA in 1990 and Howanitz et al. [2] in 2002. The spectrum of critical pa-rameters reported in these publications does not meet the require-ments of laboratory medicine in every respect.

I have therefore put together a new list of qualitative and quantitative parameters. If you think there are parameters that should perhaps be added or deleted, limits, which need changing, or notes that need to be amended, your suggestions would be most welcome.

Quantitative laboratory test results for the blood and extravascular body fluids are indicators, for example, of organic disease, metabolic disorders, diseases of the haematopoietic system, disturbances of haemostasis, abnormalities of the endocrine system, activation or insufficiency of the immune system, inflammation, infections, and autoimmune processes.

High detection sensitivity, a wide measurement range, and good to acceptable precision and accuracy, allow blood parameters to be determined in concentration ranges, which indicate that the patient is in acute danger or even a danger to others. The laboratory must report such results to the treating physi-cian immediately. For this to happen, there must be an agreement between the treating physician and the laboratory as to what constitutes a critical result that needs to be reported to him. The parameters chosen and the critical limits depend essentially on the disease prevalence expected in the clinic or practice.

The laboratory should not report a criti-cal result to the treating physician until it has been confirmed by a second deter-mination in the same sample.

The laboratory test value should be ascertained by a competent member of the laboratory (laboratory doctor, clinical chemist, senior medical laboratory tech-nician) who should discuss the result with the treating physician.

This is because influences and interfer-ence factors in the preanalytical phase, e.g. sample collection for glucose measurement using a venous catheter that had been used for glucose infusion, are not infrequently the cause of seemingly critical values. Such cases are usually clarified by the testing of another, properly collected sample.

The specified parameters and limits are taken partly from [1]. The others are based on 25 years' experience as a doctor for laboratory medicine working in a hospital.

**References:**

Kost, GJ. Critical limits for urgent clinician notification at US medical centers. JAMA 1990; 263: 704-7

Howanitz PJ, Steindel SJ, Heard NV. Laboratory critical values, policies and procedures. A College of Ameri-can Pathologists Q-probes study in 623 institutions. Arch Pathol Lab Med 2002; 126: 663-9.

**Table 1: Adult and paediatric limits of laboratory results which, after confirmation through repeat measurement in the same sample, need urgent notification of the physician**

| Parameter | Value | Note |
|---|---|---|
| Activated partial thromboplastin time (APTT) | 75 sec | Deficiency or inactivity of factor VIII, IX, XI, or XII, with risk of haemorrhage. In persons receiving heparin therapy there is a risk of haemorrhage if the APTT is more than 2.5 times higher than the upper reference limit. |
| Aminotrans-ferases | > 1000 U/l | Notification depends on the patient population of the clinic or practice in question. |
| Ammonia | > 100 mg/dl (59 mmol/l) | Risk of hepatic encephalopathy. Comatose states do not usually occur unless levels exceed 300 mg/dl (176 mmol/l). |
| Anion gap | > 20 mmol/l | Indicative of ketoacidosis or lactacidosis, uraemia, alcohol consumption, salicylate intoxication, poisoning from methanol or ethylene glycol. |
| Inorganic phosphate | < 1.0 mg/dl (0.32mmol/l)<br><br>> 9.0 mg/dl (2.9 mmol/l) | Muscle weakness, muscle pain, central-nervous symptoms such as disorientation, confusion, convulsions, coma, respiratory insufficiency with metabolic acidosis.<br><br>Occurs in acute tumour lysis syndrome and in terminal renal failure. |
| Antithrombin (AT) | < 50% | There is substantial inhibitor deficiency, which in those with elevated procoagulant activity poses a high risk of thromboembolic complications. |
| Ethanol | > 3.5 g/l (76 mmol/l)<br><br>> 3.5 % | Blood alcohol concentrations of 3-4 g/l can be fatal, even in those who are not simultaneously using medicinal products. |
| Bilirubin | > 15 mg/dl (257 mmol/l) | Hepatobiliary disease caused mainly by hepatotropic viruses and thus of infectious origin with risk of contagion. |

| Parameter | Value | Note |
|---|---|---|
| Chloride | < 75 mmol/l<br><br>>125 mmol/l | Indicative of considerable metabolic alkalosis.<br><br>Indicative of massive primary metabolic acidosis or pseudohyperchloraemia in the case of bromide intoxication. |
| Creatinine | > 7.4 mg/dl (654 mmol/l) | Acute renal failure, e.g. in multiple organ failure or sepsis. |
| Creatine kinase | > 1000 U/l | Notification depends on the patient population of the clinic or practice in question. |
| D-dimers | Positive | In disseminated intravascular coagulation (DIC), detection of D-dimers is indicative of phase II (decompensated activation of the haemostasis system) or phase III (full-blown DIC). |
| Digoxin<br><br>Digitoxin | > 2.0 mg/l (2.56 nmol/l)<br><br>> 40 mg/l (52 nmol/l) | Non-cardiac symptoms such as tiredness, muscle weakness, nausea, vomiting, lethargy, and headache and cardiac symptoms such as sinus arrhythmia, bradycardia, and various degrees of AV block. |
| Fibrinogen | < 0.8 g/l | Risk of haemorrhage. |
| Fibrin monomers | Positive | Indicative of consumption coagulopathy in disseminated intravascular coagulation, sepsis, shock, multiple injury, acute pancreatitis, and obstetric complications. |
| Glucose | < 45 mg/dl (2.5 mmol/l)<br><br>> 500mg/dl<br><br>(27.8 mmol/l) | Neuroglycopenic symptoms, which can range from impairment of cognitive functions to loss of consciousness.<br><br>Diabetic coma due to insulin deficiency. Development of osmotic diuresis with severe exsiccosis and diabetic ketoacidosis (b-hydroxybutyrate > 5 mmol/l, standard bicarbonate < 10 mmol/l). |

| Parameter | Value | Note |
|---|---|---|
| Haemoglobin | < 6.6 g/dl<br><br>> 19.9 g/dl | Supply of oxygen to the myocardium inadequate.<br><br>Corresponds to haematocrit of 61% and leads to hyperviscosity syndrome. |
| Lactate | > 45 mg/dl (5.0 mmol/l) | Indicator of type A hyperlactataemia, which is caused by an inadequate supply of oxygen to the tissue. Pyruvate is no longer metabolised oxidatively, but reductively. |
| Lactate dehydrogenase | > 1000 U/l | Notification depends on the patient population of the clinic or practice in question. |
| Leukocyte count | < 2000/ml<br><br>> 50,000/ml | High risk of infection if the granulocyte count is < 500/ml.<br><br>Indicative of leukemoid reaction, e.g. in sepsis, or of leukemia. |
| Lipase | > 700 U/l | Indicative of acute pancreatitis. |
| Magnesium | < 1.0 mg/dl (0.41 mmol/l)<br><br>> 4.9 mg/dl (5.0 mmol/l) | Characteristic symptoms are paresthesias, cramp, irritability, and athetoid tetany. The patient often shows cardiac arrhythmia in conjunction with hypokalemia; arrhythmia is intensified by digitalis.<br><br>Reduction of neuromuscular impulse transmission, resulting in sedation, hypo-ventilation with respiratory acidosis, muscle weakness, and reduced tendon reflexes. |
| Myoglobin | > 110 mg/l | Myocardial infarction should be suspected in patients with angina pectoris. |

| Parameter | Value | Note |
|---|---|---|
| Osmolality | < 240 mOsm/kg H2O<br><br>> 330 mOsm/kg H2O | Cellular oedema with an increase in cell volume and development of neurological-psychiatric symptoms.<br><br>Cellular water loss and intracellular increase in osmotically active substances, which do not permeate the cell membrane. Result: central symptoms and coma. |
| Osmolar gap | > 10 mOsm/kg H2O | Indicative of intoxication from non-electrolytes, which increase plasma osmolality, such as ethanol, methanol, ethylene glycol, isopropanol, and dichloromethane. |
| pCO2 | < 19 mm Hg (2.5 kPa)<br><br>> 67 mm Hg (8.9 kPa) | Hyperventilation<br><br>Hypoventilation |
| pH | < 7.2<br><br>> 7.6 | Such pH values are characteristic of severely decompensated acidosis or alkalosis. Values < 7.20 and > 7.60 are life-threatening. |
| pO2 | < 43 mm Hg (5.7 kPa) | Such values correspond to a haemoglobin oxygen saturation of less than 80% and are to be regarded as life-threatening. |

| Parameter | Value | Note |
|---|---|---|
| T4, free<br><br>T3, total | > 35 ng/l (45 pmol/l)<br><br>> 30 mg/l (46 nmol/l) | Indicative of thyrotoxicosis, a condition detectable clinically and in laboratory tests; the tissues are exposed to too high a thyroid hormone concentration and react to this. Possible causes are: Graves' disease, trophoblastic tumour, hyperfunctional adenoma, toxic nodular goitre, and, in rare instances, overproduction of TSH. |
| Thromboplastin time (TT) | > 27 sec (approx. 50%) | Decrease in the vitamin K-dependent factors II, VII, and X or in factor V. Since all these factors are synthesized in the liver, a decrease in the TT to values below the specified level indicates a considerable disturbance of synthesis. In persons receiving coumarin therapy, there is a risk of haemorrhage if the TT is < 15% – which corresponds roughly to an INR of > 4. |
| Platelet count | < 20,000/ml<br><br>> 1 million/ml | Risk of haemorrhage. Exclude EDTA-induced thrombocytopenia.<br><br>Risk of thrombosis. |
| Troponin | > 0.1 mg/l | Indicative of myocardial infarct or unstable angina pectoris. |
| Uric acid | > 13 mg/dl (773 mmol/l) | Acute urate nephropathy with tubular blockade and renal failure. The uric acid/creatinine ratio in spontaneous urine in such cases is > 1.0 (mg/mg). |
| Urea<br><br>BUN | > 214 mg/dl (35.6 mmol/l)<br><br>> 100 mg/dl (35.6 mmol/l) | Indicative of acute renal failure; unlike pre-renal and post-renal kidney failure, no disproportionate increase in urea compared to creatinine in serum. |

## Table 2: Critical limits of qualitative laboratory results which must be reported to the treating physician immediately

### Cerebrospinal fluid

- Increased cell count
- Leukocytosis, tumour cells
- Glucose lower than in serum
- Lactate > 20 mg/dl (2.2 mmol/l)
- Detection of pathogens in Gram stain or agglutination test

### Urine · Strongly positive test strip reaction for glucose and acetone

- Red cell casts or > 50% dysmorphic erythrocytes
- Severe haemoglobinuria (no erythrocytes on microscopic examination)
- Detection of drugs

### Differential blood count · Leukemoid reaction

- Suspected leukemia
- Suspected aplastic crisis
- Sickle cells
- Malarial parasites

### Microbiology · Detection of pathogens in Gram staining of blood culture or of exudates and transudates of body cavities

- Antigenic detection of pathogens with rapid tests such as latex agglutination, immunofluorescence, or immunoassay, e.g. group B streptococci, legionella, Pneumocystis carinii, Cryptococcus, hepatitis B
- Detection of acid-fast bacilli or detection of M. tuberculosis after amplification (PCR)
- Cultural detection of salmonellae, shigella, Campylobacter, C. difficile, C. perfringens, N. gonorrhoeae, B. pertussis, N. menin-gitidis, C. diphtheriae, and pathogenic fungi such as Aspergillus, Blastomyces, Coccidioides, Histoplasma, and Cryptococcus
- Detection of HIV antibodies

**Table 3: Neonatal quantitative limits of laboratory results which, after confirmation through repeat measurement in the same sample, need urgent notification by the physician.**

| Parameter | Value | Note |
|---|---|---|
| Bilirubin | > 14 mg/dl (239 mmol/l) | On first day of life, e.g. in hemolytic disease of the newborn; risk of kernicterus. |
| C-reactive protein | > 5mg/l | Indicative of neonatal sepsis. |
| Glucose | < 30 mg/dl (1.7 mmol/l)<br><br>> 325 mg/dl (18 mmol/l) | Hypoglycemia, caused, for example, by a congenital metabolic disorder or hyperinsulinism due to maternal diabetes mellitus. Glucose concentrations < 25 mg/dl (1.3 mmol/l) should be treated by parenteral administration of glucose.<br><br>Urgent clarification of pathogenicity required. |
| Hematocrit | < 33% (L/L)<br><br>>71% (L/L) | Indicative of marked anemia with an inadequate supply of oxygen to tissue.<br><br>Hyperviscosity of the blood with increased circulatory resistance. |
| Hemoglobin | < 8.5 g/dl<br><br>> 23 g/dl | Risk of multiorgan failure, especially if the patient has a combination of ischemia and hypoxia.<br><br>Abnormal flow kinetics (hyperviscosity) with increased circulatory resistance and an increased load on the heart. |
| Igm | > 20 mg/dl | A cord blood IgM concentration above the limit can be linked to an intrauterine infection. |
| Potassium | < 2.6 mmol/l<br><br>[3] 7.7 mmol/l | Occurrence of neuromuscular symptoms with hyporeflexia and paralysis of the respiratory muscles.<br><br>Clinical consequences are heart-rhythm disturbances, weakness of the skeletal muscles, and respiratory paralysis. |
| Leukocyte count | < 5,000/ml<br><br>> 25,000/ml | Values below and above these limits can be indicative of neonatal sepsis. |
| pO2 | < 37 mm Hg (4.9 | Drop in hemoglobin oxygen saturation to below 85%. |